169. The cartridge of claim 168 wherein said mechanical agitator comprises a stir bar.

170. The cartridge of claim 168 wherein said mechanical agitator comprises a piston.

171. The cartridge of claim 164 wherein said sample storage container comprises a reservoir, and wherein said resuspension means comprises a mechanical agitator positioned outside of said reservoir and vibrationally coupled with said reservoir.

REMARKS

The Amendments

All pending claims have been canceled, and new claims 123-171 substituted therefor. The new claims parallel the elected claims as filed in the parent application with the following exceptions: Claim 123 does not specify a resuspension pump interface. The resuspension pump interface is now specified in new claim 129. Claim 123 further specifies that the first analysis channel is in fluidic communication with the first analysis region. Support is found, e.g. in Figure 1.

Claims 123 and 164 specify that the channels are nonporous. Support is inherent in the specification at page 2 describing how particles in a sample fluid sediment out and may be resuspended by reverse or continuous flow and the sample thereby reconstituted. Support is also found in the drawings which do not indicate pores in the channel. Support for the word "nonporous" is inherent because the fact that the channels must be made of a nonporous material is the "necessary and only reasonable construction" that can be put on the description of the channels (*Alco Standard v. Tennessee Valley Authority*, 1 USPQ2d 1337 (CAFC 1986)). If the channels were made of a porous material, they would not be

able to allow sedimenting out of particles followed by resuspension and reconstitution of the sample fluid. If some of the sample fluid had leaked out through pores in the channels, it could not be reconstituted. Thus, the necessary and only reasonable construction is that the channels are nonporous. Support for the term "nonporous" is therefore inherent in the specification. Claims 123 and 164 specify that the analysis region comprises access for detection means. Support is found, e.g. at page 11, line 21 through page 12, line 8.

New claim 124 specifies that the channels are made using first, second and third sheets, the second sheet having a cutout therein. Support is found, e.g., in Figure 4 and page 10, last partial paragraph, and page 18, last full paragraph.

Claim 171 (corresponding to as-filed claim 105) refers to "storage container" rather than "storage compartment" for better antecedent basis.

<u>The Rejection Under Section 102</u>

In the final Office Action in the parent application issued July 17, 2000, claims 1-3, 6-10 and 98-100 were rejected as anticipated by Bormann et al. (US Patent 5,601,727). The new claims corresponding to the rejected claims appear to be 123, 125, 126, 129-134, and 164-166. The Office Action states:

> Bormann teaches a fluidic sample analysis cartridge for analyzing a particle-containing liquid sample comprising a sample inlet 11 having a shut-off interface, convoluted sample storage channels 20-22 comprised entirely of solid material (col. 7, line 57- col. 9, line 57) in fluidic connection with the inlet, a resuspension pump 90 interface in fluidic connection with the storage channel and having a first analysis region 18. Bormann explains the fluid processing system may also include a valve

located within or on at least one of the convoluted sample storage samples [channels?] (column 6, lines 22-67 and column 7, lines 1-35, Figures 1-3).

The Office Action further states in response to applicants' previous arguments:

> Applicant's arguments have been fully considered but they are not persuasive. In response to the previous Office Action, applicant argues that Bormann et al. (USP 5,601,727) teaches channels which have at least one permeable side and the present application teaches a storage channel which is formed entirely of "solid" material. Examiner points out that such a limitation does not exclude the use of permeable walls since the limitation "solid", as defined by the specification on pages 19, lines 9-24, refers to "a plurality of sheets laminated together or the channels can be etched in a silicon substrate and covered with a cover sheet, which can be a transparent cover sheet". Further, "The layers are preferably fabricated from substantially rigid materials, examples of substantially rigid plastics include cellulose acetate, polycarbonate, methylmethacrylate and polyester". The pore diameters of the materials are not defined. The Bormann device clearly states that the separation membrane can be made from a polymer such as polyester (col. 9, lines 47-51). Therefore as defined in the specification, the Bormann reference clearly discloses the present invention. Further, it is inherent in the Bormann device that the channels 20-22 are contained within a solid outer channel or the fluid would simply flow outside of the housing 10, see Fig. 3.
>
> Applicant argues that the Bormann patent makes no reference to a "resuspension pump" as claimed. Examiner points out that the specification defines a "resuspension pump as a "syringe pump" on page 11 lines 14-20 and Fig. 5 and claim 8, which is clearly taught at col. 6, lines 36-37 and Fig 2 of Bormann et al. Applicant argues that a "shut-off interface" is not taught by Bormann et al. Examiner directs Applicant's attention to col. 6, lines 49-52 which discloses a seal. Applicant argues that the "analysis channel" is merely a conduit Examiner points out that the "analysis channel" 24 is simply a conduit as seen in Fig 9 in the present application. Applicant argues that the "analysis region" is a collection bag which provides no means for interrogation by analytical equipment. This argument is not germane to the issue since applicant has not included such analytical equipment within claims 1 or 98.

Bormann et al. does not appear to teach a device for performing analysis. It is a blood product separation device. See col. 5, lines 9-12. The device contains convoluted channels, but these do not appear to be "storage" channels. The channels of the Bormann et al. device are designed with at least one porous wall so that rather than storing liquid, they allow liquid to exit out of the channel. See col. 8, lines 9-16 which state:

> [T]he channels are defined by three sides which are substantially impermeable to and substantially unreactive with the biological fluid, and one side, i.e., defined by the **separation medium**, that is **permeable** to the biological fluid. Alternatively, the channels may be defined by two substantially impermeable and substantially unreactive sides and **two permeable** sides. [Emphasis added.]

The term "separation medium" is defined at col. 3, lines 50-52 as follows:

> A separation medium refers to a **porous** medium through which one or more biological fluids pass and which separates one component of the biological fluid from another. [Emphasis added.]

Although the Bormann et al. device includes a pump, it does not include a "resuspension" pump because it does not allow particles to sediment and then resuspend them as in the present invention. Further, the device does not have a first analysis region. Element 18 is a "first satellite bag," (col. 6, lines 38-39) and no analysis takes place within it. The cited device also does not appear to have a "shut-off interface" as required by claims 123-163.

Since Bormann et al. lacks elements of the present claims, namely, a channel which is "nonporous" and which is a "storage" channel, and since it is not an "analysis" cartridge and does not have an "analysis region," the reference does not anticipate the present claims, all of which recite these elements which are missing in the reference. The cited device also does not appear to have a "shut-off interface" as required by claims 123-163. Withdrawal of the rejection is therefore respectfully requested.

The Patent Office appears to interpret a "solid" material as one which can be porous. While this appears to be contrary to the ordinary meaning of the term "solid," to expedite prosecution, applicants have amended the claims to specify that the channels are "nonporous." Further, the Patent Office seems to be taking the position that a "channel" of Bormann et al. is a structure having a separation medium **within** it. This is contrary to the definition of "channel" used by Bormann et al. (quoted above) which uses the separation medium to define one or two of the channel walls. Further, the Bormann et al. channel cannot by any stretch of the imagination be called a "storage channel" as claimed herein because it does not store the fluid within it so that it can be reconstituted without agglomeration, but rather separates liquid from the fluid and does not allow the fluid to be reconstituted.

The Patent Office appears to be interpreting the syringe pump of the Bormann et al. device as a "resuspension pump" because it is a syringe like that used in the present invention as a pump for resuspension. However, it is pointed out that the Bormann et al. syringe cannot be a "resuspension pump" because the remainder of the device is not configured to allow it to "resuspend" particles which have settled out. The devices must be viewed as a whole rather than comparing each element in a vacuum. In the present device, a syringe can be a "resuspension pump." In the reference it cannot.

The Patent Office appears to be interpreting a generic disclosure that the conduits of Figure 1 can be equipped with a seal as equivalent to the "sample inlet having an inlet shut-off interface" claimed herein. However, it is pointed out that the conduits shown in Figure 1 of the reference are external to the separation device 200, and there does not appear to be a teaching in the reference that the inlet to the separation device is equipped with a seal. Thus the reference does not show a "sample inlet shut-off interface."

The Patent Office appears to be correct that the analysis channel 24 shown in Figure 8 of the present application is a conduit. However, applicants are correct that the analysis region identified in the Office Action (element 18 of the reference) is merely a collection bag, not an analysis region. No means for analysis are specified, nor any access for detection means. Although it is believed that access to detection means is an inherent property of any "analysis region," claims 123 and 164 have been amended to specify the presence of access for detection means in order to expedite prosecution.

The Obviousness Rejection over Bormann et al. and WO 97/39338

Claims 4-5 and 11-21 were rejected as obvious over Bormann et al. and WO 97/39338, referring to the first Office Action. These claims appear to correspond to present claims 127-128 and 135-145. The first Office Action stated:

> Bormann as discussed above, does not teach the width of the storage channel between about 25 and 2,000 micrometers. However, WO 97/3933 8 does teach the width of the storage channel between about 20 and 2,000 micrometers (page 8, line 17). It would have been obvious at the time of the invention to have included in the fluid sample analysis system of Bormann the range of widths of the storage channel as taught by WO 97/39338. This narrow width of the channel makes diffusion occur more rapidly, and thus detection can be done more rapidly (page 8, lines 2 1-22).

It is submitted that no *prima facie* case of obviousness has been made out. There is no reason why one skilled in the art would be motivated to combine a macroscale blood separation device like that of Bormann et al. with a microscale analytical device like that of WO 97/39338.

To establish a *prima facie* case of obviousness, the Patent Office must show "some objective teaching in the prior art or that knowledge generally available to one of ordinary

skill in the art would lead that individual to combine the relevant teachings of the references." *In re Fine,* 5 USPQ2d 1096 (Fed. Cir. 1988). There is no suggestion to combine, however, if a reference teaches away from its combination with another source. *Id.* 1599. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant . . . [or] if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *In re Gurley*, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). If when combined, the references "would produce a seemingly inoperative device," then they teach away from their combination. *In re Sponnoble*, 160 USPQ 237, 244 (CCPA 1969); see also *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984) (finding no suggestion to modify a prior art device where the modification would render the device inoperable for its intended purpose).

In the present instance, the skilled worker in search of a means for preventing agglomeration of particles and resuspending them so as to reconstitute the fluid--a problem solved by the present invention--would not be led to combine the straight diffusion channel of WO 97/39338 with the convoluted channel of Bormann et al. because the porous sides of the Bormann et al. channels would allow fluid to leak away so that the sample fluid could not be reconstituted. Thus, the combination of references would be "unlikely to be productive of the result sought by the applicant." The combination of references therefore teaches away from the present invention, and thus no *prima facie* case of obviousness has been, or can be made out. Withdrawal of the rejection is respectfully requested.

The Obviousness Rejection over Bormann et al. and Chemelli (USP 5,288,463)

Claims 22-39 have been rejected as obvious over Bormann et al. and Chemelli (USP 5,288,463) for reasons set out in the first Office Action These claims appear to correspond to new claims 146-163. The first Office Action stated:

> Bormann as discussed above, does not teach a reagent inlet in fluid communication with the first analysis channel between the storage channel and the first analysis region. However, Chemelli does teach a reagent inlet 56 in fluid communication with the first analysis channel 40 between the storage channel 44 and the first analysis region 41. It would have been obvious at the time of the invention to have included in the liquid analysis system of Bormann a reagent inlet in fluid communication with the first analysis channel between the storage channel and the first analysis region, in order to create the desired chemical reactions required for analysis before entering the detector.

While it appears that Chemelli does have a reagent inlet in fluidic connection with an analysis region, it would not have been obvious to combine Chemelli with Bormann et al. Bormann et al., as discussed above, is a blood separation device, not a blood analysis device. One skilled in the art would not be likely to combine a blood separation device with a PCR amplification device such as that of Chemelli if he were seeking a way to process and store blood without particle agglomeration. Again, the porous sides of the Bormann et al. channels would not lend themselves to storing and reconstituting a fluid, the purpose of the present invention. No *prima facie* of obviousness has been made out. The combination of references would not be operable for applicants' purpose, and thus there is no motivation to combine them; rather in combination the references teach against applicants' claimed invention. Withdrawal of the rejection is respectfully requested.

Obviousness Rejection over Bormann et al. and Miyake et al.

Claims 101-105 have been rejected as obvious over Bormann et al. in view of Miyake et al. for the reasons set forth in the first Office Action. These claims appear to correspond to new claims 167-171. The first Office Action stated:

> Bormann as discussed above does not teach a resuspension means comprising an ultrasonic vibrator acoustically coupled to the reservoir. However, Miyake does teach a resuspension means comprising an ultrasonic vibrator 103 acoustically coupled to the reservoir 301 (columns 1-2, Figures 2-3). It would have been obvious at the time the invention was made to include in the fluid sample analysis of Bormann a resuspension means comprising an ultrasonic vibrator as disclosed by Miyake. This allows for reduced amounts of sample and reagent needed to be mixed effectively together. Thus, the amount of sample and reagent to be fed into a reaction vessel can be of the quantities required only for a chemical analysis and measurement, with a result that the sizes of the reaction vessels can be reduced (column 3 lines 24-30).

Again, it is pointed out that it would not be obvious to add resuspension means to the separation device of Bormann et al. Bormann et al. intends to separate components, not remix them (resuspend particles that have settled out). Further, with respect to claims 168-170, the Miyake et al. reference teaches away from the use of agitating means within the reaction region (col. 2, lines 52-53) to avoid contaminating subsequent reactions. No *prima facie* case of obviousness has been made out because there is no motivation to combine the references. It is not understood how combining an ultrasonic mixing means with the Bormann et al. separation device would allow for reduced amounts of sample and reagent as asserted in the Office Action, especially since no reagent is mentioned in Bormann et al. Withdrawal of the rejection is respectfully requested.

CONCLUSION

This application appears to be in condition for allowance. Passage to issuance is respectfully requested. The application filing fee has been calculated based on the claims presented herein. No other fee is believed to be due. If this is incorrect, however, please charge any required fee or extensions of time to Deposit Account No. 07-1969.

Respectfully submitted,

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